Long-term results of coronary artery bypass grafting procedure in the presence of left ventricular dysfunction and hibernating myocardium

Roberto Lorusso, Giovanni La Canna, Claudio Ceconi, Valentino Borghetti, Pasquale Totaro, Giovanni Parrinello, Giuseppe Coletti, Gaetano Minzioni

Cardiac Surgery Division, Civic Hospital, 25125 Brescia, Italy
Cardiology Division, Civic Hospital, 25125 Brescia, Italy
Nuclear Cardiology Division, Civic Hospital, 25125 Brescia, Italy
Biomedical Statistics, University of Brescia, Brescia, Italy

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Abstract

Objective: Long-term left ventricular (LV) performance and patient outcome after coronary artery bypass grafting (CABG) procedure in the presence of depressed LV function and hibernating myocardium (HM) have been poorly determined. Therefore, we prospectively evaluated patients undergoing CABG with severe LV dysfunction and HM to elucidate postoperative prognosis. Methods: We enrolled 120 consecutive patients undergoing CABG with severe LV dysfunction and HM as assessed by dobutamine echocardiography and by rest-redistribution radionuclide (Thallium-201) study. Mean patient age was 60 ± 9 years (range 31–77 years). Mean preoperative LVEF was 28% ± 9% (range 10–40%). All patients underwent echocardiographic study to assess LV recovery of function intraoperatively, prior to hospital discharge, at 3 months, at 1 year, and yearly during the follow-up. Univariate and multivariate analysis were performed to evaluate predictors of postoperative survival. Results: There were 2 hospital (1.6%) and 15 late (12.5%) deaths, mainly for heart failure, leading to an actuarial survival of 80 ± 6% and 60 ± 9% at 5 and 8 years, respectively. LVEF significantly improved perioperatively (from 28% ± 9% to 40% ± 2%, P < 0.01). Increase in LVEF, however, was gradually offset over the time (EF of 33% ± 9%, 32% ± 8%, and 30% ± 9% at 3 months, and 12 months, and 8 years after surgery, respectively). Furthermore, patients who experienced limited LV functional recovery perioperatively had a more remarkable decline of LVEF thereafter, and suffered from recurrence of heart failure symptoms (freedom from heart failure 82 ± 5% and 60 ± 8% at 4 and 8 years respectively). Advanced preoperative NYHA Class, and age were independent risks factors for reduced postoperative survival. Preoperative angina and use of arterial conduits apparently did not influence patient morbidity and mortality at long term. Conclusion: CABG procedure in the presence of HM enhances LV recovery of function and has a favourable prognosis. Functional benefit of the left ventricle, however, appears to be time-limited, despite remarkable improvement in patient functional capacity. Advanced preoperative heart failure, minimal perioperative improvement of LVEF, and age account for a poor long-term prognosis. © 2001 Elsevier Science B.V. All rights reserved.

Keywords: Coronary artery bypass grafting; Hibernating myocardium; Left ventricular dysfunction; Ischemic cardiomyopathy; Postoperative prognosis

1. Introduction

Surgical revascularization in patients with severe left ventricular (LV) dysfunction provides survival benefit as compared to medical therapy at long term [1,2]. Despite recovery of impaired myocardial function has been shown after coronary artery bypass grafting (CABG) [1–7], contractile dysfunction of the LV remains a negative determinant of postoperative outcome [2,5,8]. Recently, the presence of akinetic yet viable myocytes, peculiar condition denominated hibernating myocardium [9] (HM), showed to characterise subgroup of patients having higher probability of improvement in LV function and more favourable postoperative survival after revascularization [10–15]. The likelihood of predicting reversible myocardial dysfunction has gained enormous relevance among the investigators, and techniques capable of identifying HM have been, therefore, a critical component of the diagnostic process to select patients for conventional methods of myocardial revascularization despite advanced LV dysfunction, with important implications either on early and on late postoperative results.
or allocation of alternative therapies [15]. Preoperative clinical condition has been also associated with postoperative outcome, being the preoperative presence of angina a positive predictor of improved life expectancy despite impaired LV performance as compared to patients with heart failure symptoms, and usually linked to viable and recoverable myocardium [1]. However, despite the impact of depressed LV function on CABG results has been largely highlighted and the importance of patient selection variably underscored, scarce information are available on the actual outcome of CABG in patients affected by LV dysfunction and HM. The long-term benefits of such a surgical therapy in this peculiar setting of myocardial compromise are, therefore, still undefined as are the potential predictors of unfavourable late LV function and patient survival. Our study prospectively enrolled patients characterised exclusively by LV impairment and HM. The results of such a follow-up are herein reported.

2. Methods

From February 1989 until April 2000, 120 consecutive patients were enrolled for this prospective study. Inclusion criteria consisted of presence of severe LV dysfunction (EF ≤ 40%), evidence of ample segments of hibernating myocardium involving at least the territories of the anterior descending coronary artery (LAD), graftable coronary vessels, elective surgery, absence of acute myocardial infarction (less than 1 month prior to surgery). Preoperative patient characteristics are summarised in Table 1. Heart failure symptoms (NYHA Class III or IV) were present in 43% of patients preoperatively. Diabetes mellitus was present in 29 patients (34.8%). Concomitant mitral valve insufficiency was present in 29 patients (trivial in 10 patients, mild in 15 patients, moderate in two patients and severe in two patients, respectively), requiring mitral valve repair (annular remodelling with prosthetic ring) in three patients. One patient had had associated aortic valve disease and had undergone aortic valve replacement. Ten patients had had mechanical circulatory support (intraaortic balloon counterpulsation) prior to CABG procedure, but were not under mechanical assistance at the time of surgery. Two patients had had implantable defibrillator (AICD) implantation prior to CABG procedure due to malignant ventricular arrhythmia. One-vessel disease was present in five patients, two-vessel disease in 37 patients, and tree-vessel disease in 78 patients, respectively.

2.1. Assessment of hibernating myocardium

All patients included in this study had marked LV dysfunction (EF below 40% at transthoracic/transesophageal echocardiography and confirmed at left ventricular angiography) and exhibited HM. The presence of akinetic yet viable myocardium was determined initially by transthoracic echocardiography followed by transesophageal assessment. The evidence of preserved myocyte functional activity was obtained by transesophageal echocardiography stress test using dobutamine infusion according to dosages and infusion rates as previously described [16]. Patients were also submitted to radionuclide assessment. Rest-redistribution technique with Thallium-201 was used to differentiate necrotic areas from hypoperfused, but viable zones according to protocol previously reported [16]. All patients were then submitted to coronary angiography to assess extent of coronary artery disease and anatomy. All coronary arteries presenting stenosis greater than 70% were considered for revascularization. Anatomical details regarding peripheral disease and vessel diameter were also factors screened for surgical inclusion.

2.2. Surgical management

Because of a wide time span, surgical strategies varied along the study course, particularly with regards to myocardial protection. Indeed, cardiac arrest was induced by different techniques, as described in Table 2. A change in CABG conduits also occurred during the study period since patients in the first series underwent myocardial revascularization with vein conduits only (36 patients), whereas arterial graft (internal thoracic artery) was used almost routinely to perfuse the LAD territories in the most recent series series (84 patients). Complete coronary revascularization was achieved in almost all patients of operated patients (2.8 ± 0.8 grafts/patient).

Table 1
Preoperative patient characteristics

| Patients | 120 |
| Age      | 60 ± 9 (range 31–77 years) |
| Gender   | 108 Male, 12 Female |
| NYHA Class | I 60, II 21, III 25, IV 5 |

Preoperative myocardial infarction

| Anterior | 60 |
| Lateral  | 19 |
| Inferior | 61 |
| Posterior | 6 |
| Multiple location | 44 |

Ventricular arrhythmia

| 15 (2 AICD) |

Angina

| 69 (57%) |

Heart failure symptoms

| 42 (35%) |

Angina/heart failure Symptoms combined

| 9 (8%) |

LVEF

| 28 ± 9 (range 10–40%) |

Previous acute pulmonary edema

| 35 |

Associated cardiac procedures

| Mitral valve repair 3, Aortic valve replacement 1 |
2.3. Postoperative follow-up

Intraoperatively, all patients underwent echocardiographic control (transesophageal and epicardial) to detect immediate effects of CABG. All patients were also studied by transthoracic echocardiography by expert cardiologists prior to hospital discharge, at 3, 12 months after surgery and on an yearly basis thereafter. A limited number of patients underwent postoperative coronary angiography and radio-nuclide assessment between 6 and 12 months from surgery, whose results are not herein reported because of the preliminary nature of results. All patients had appropriate medical therapy (ACE-inhibitors, diuretics), and the majority were on Beta-blockers. No specific pharmacological protocol was carried out as regards to statin or antiarrhythmic therapy.

2.4. Statistical analysis

All values are presented as mean ± standard deviation. Linear mixed models for repeated measures were performed to predict postoperative trend of LV function. Univariate and multivariate analysis were performed to disclose predictive variables for patient survival. Variables considered for univariate and multivariate analysis were as follows: patient age and gender, history of and location of previous myocardial infarction, primary symptoms (angina or heart failure symptoms), use of left internal thoracic artery (LITA) or vein grafts for the anterior descending coronary artery, LVEF, pulmonary hypertension, diabetes, NYHA Class, percentage of intraoperative increase in LVEF, number of distal anastomosis, extracorporeal circulation and aortic cross-clamping times, route and type of cardioplegia.

3. Results

Mean follow-up was 3.8 ± 6 years (range from 3 months to 9 years) and no patient was lost during follow-up. There were two hospital (1.6%) and 15 late (12.5%) deaths, leading to an actuarial survival of 84 ± 6% and 60 ± 9% at 4 and 8 years, respectively (Fig. 1). Causes of postoperative mortality are listed in Table 2.

![Postoperative Survival](image)

**Fig. 1.** The figure shows estimated survival (Kaplan–Meyer) probabilities of the 120 patients with impaired LV function and hibernating myocardium following CABG procedure. Dashed lines enclose the 70% confidence limits.

<table>
<thead>
<tr>
<th>Early Causes</th>
<th>Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>LCOS</td>
<td>1</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>1</td>
</tr>
<tr>
<td>Late Causes</td>
<td></td>
</tr>
<tr>
<td>Cardiac related</td>
<td></td>
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<tr>
<td>Chronic heart failure</td>
<td>5</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>1</td>
</tr>
<tr>
<td>Sudden death</td>
<td>3</td>
</tr>
<tr>
<td>Non-cardiac related</td>
<td></td>
</tr>
<tr>
<td>Cancer</td>
<td>1</td>
</tr>
<tr>
<td>Diabetes-related complications</td>
<td>1</td>
</tr>
<tr>
<td>Cerebral hemorrhage</td>
<td>1</td>
</tr>
<tr>
<td>Unknown</td>
<td>3</td>
</tr>
</tbody>
</table>

Table 2 Causes of postoperative mortality

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The majority of late deaths were due to chronic heart failure and occurred in patients with preoperative end-stage heart failure and more severe impairment of LV function. Remarkably, sudden death did not represent a frequent postoperative event in this study population, with only three arrhythmic-related deaths during follow-up, despite frequent premature ventricular beats present at the preoperative electrocardiogram and lack of prophylactic medical therapy to prevent arrhythmia postoperatively.

LVEF significantly improved perioperatively (from 28 ± 9% to 40 ± 2%, P < 0.01). Increase in LVEF, however, was gradually offset postoperatively (EF of 33 ± 9%, 32 ± 8%, and 30 ± 9% at 3 months, at 12 months, and at 8 years after surgery, respectively) (Fig. 3). Noteworthy, patients who experienced limited LV functional recovery perioperatively had a greater decline of LVEF thereafter, and suffered from recurrence of heart failure symptoms and hospital readmissions. Freedom from recurrence of heart failure was 82 ± 5% and 60 ± 8% at 4 and 8 years, respectively (Fig. 2). Limited benefit of CABG on LVEF and prevention of heart failure recurrence was more frequently observed in patients with preoperative advanced heart failure who, therefore, had temporary relief of heart failure symptoms and transient improvement of LV contractility with subsequent deterioration of clinical conditions and LV performance (Fig. 3). At follow-up, survivors showed a substantial improvement in functional capacity as compared to preoperative status since patient New York Heart Association (NYHA) Class improved at 4 years postoperatively (from 43% to 24% of patients in NYHA Class III or IV), and gradually declined thereafter (35% of patients in NYHA Class III or IV at 8 years). This condition was also corroborated by the need of medical therapy maintenance (40% of patients) or increase (30% of patients) at latest follow-up as compared to preoperative therapeutic regimen.

Ventricular arrhythmia or other rhythm disturbances did not represent a frequent complication in this series. Only one patient required AICD implantation postoperatively following an episode of ventricular tachycardia recorded at the Holter monitoring and subsequent electrophysiological study which indicated the need for the antitachy device.

The use of arterial conduits for (LAD) revascularization did not apparently exert additional benefit to postoperative outcome. Indeed, survival, heart failure or angina recurrence rate were not modified by the use of left thoracic artery to revascularize the LAD territories (Fig. 4), although postoperative evaluation was performed with a limited mean follow-up. Repeated revascularization (PTCA) because of recurrence of angina was necessary only in three patients. No repeated CABG was performed along the follow-up. In terms of predictors of postoperative outcome, univariate analysis showed that ECC and aortic cross-clamping times, together with advanced symptoms of heart failure and age were predictive of unfavourable outcome, whereas Cox model of multivariate analysis showed that only advanced preoperative NYHA Class and age were risks factors for reduced postoperative survival (Table 3). Preo-
perative symptoms had variable impact on postoperative survival. Indeed, patients who were particularly compromised preoperatively (NYHA Class III or IV) had worse prognosis, whereas the presence of preoperative angina did not influence patient survival or the recurrence of heart failure (Fig. 5).

4. Discussion

This study showed that CABG procedure in patients affected by depressed LV function (LVEF ≤ 40%) and characterised by the presence of HM has favourable, but still not optimal prognosis at long term. We found that

Fig. 3. This figure shows the survival (A) and heart failure recurrence (B) probability after coronary artery bypass according to different degree of preoperative impaired LVEF. There was a reduced life expectancy at mid-term, whereas heart failure occurred more frequently at late follow-up in patients with worse preoperative LVEF. LVEF, left ventricular ejection fraction.
surgical revascularization of HM enhances LV recovery of function and ensures acceptable long-term survival. However, perfusing viable myocardium may exert temporary benefit in regards to LV functional improvement, particularly in patients who showed limited perioperative increase in LVEF. Heart failure progression was also shown to be partially reversed after CABG mainly in patients with LV not severely compromised, but recurrence of heart failure symptoms was not completely prevented and did occur mainly in patients with low preoperative LVEF or markedly reduced functional capacity. This clinical series also demonstrated that the use of arterial conduits to revascularise the LAD territories did not influence patient morbidity and mortality at long term. Myocardial revascu-

Fig. 4. The influence of the use of LITA (yes) on patient survival (A) and freedom from heart failure (B) is shown. No substantial impact of the use of arterial conduit for reperfusing the anterior descending coronary artery territories could be found up to 9 years from surgery. LITA, left internal thoracic artery.
Table 3
Univariate and multivariate analysis for predictors of postoperative survival

<table>
<thead>
<tr>
<th></th>
<th>Univariate</th>
<th>Multivariate</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Coef  SE  Z  P</td>
<td>Coef  SE  Z  P</td>
</tr>
<tr>
<td>NYHA Class</td>
<td>0.87  0.39  2.18  0.02*</td>
<td>0.78  0.36  2.13  0.03*</td>
</tr>
<tr>
<td>Age</td>
<td>0.22  0.09  2.31  0.02*</td>
<td>0.24  0.11  2.11  0.03*</td>
</tr>
<tr>
<td>ECCT</td>
<td>0.04  0.01  2.57  0.01*</td>
<td>NS</td>
</tr>
<tr>
<td>AoCCT</td>
<td>0.08  0.03  2.81  0.004*</td>
<td>NS</td>
</tr>
</tbody>
</table>

* NYHA, New York Heart Association; ECCT, Extracorporeal circulation time; AoCCT, Aortic cross-clamp time; NS, not significant; se, standard error; *P < 0.05 significant.

larization of ischemic cardiomyopathy also showed to potentially influence mode of death, with few terminal arrhythmic events at late outcome.

4.1. Assessment of hibernating myocardium and patient selection

Myocardial akinesis is not an irreversible condition in coronary artery disease. Indeed, the presence of functional myocardial inactivity has been shown to be associated, in particular conditions, with preserved myocyte structure and ‘freezed’ contractile function. This condition, denominated ‘hibernating’ myocardium, represents a sensitive predictors of recovery once blood perfusion has been restored in these zones [9–15]. The prevalence of patients affected by marked compromise of LV function associated with hibernating myocardium may be as high as 50% of the total population having ischemic cardiomyopathy [17], clearly underlining the relevance of identifying this peculiar myocardial condition in therapeutic decision making.

However, predicting the likelihood of myocardial recovery and postoperative prognosis of patients undergoing coronary artery bypass with depressed LV function and HM remains a challenge [18]. Noninvasive tests to establish the presence and the amount of HM have shown to be paramount for accurate patients selection and more favourable postoperative results to be achieved [11,12,14,15,17], but are still under refinement [18,19]. Apparently, functional tests (that is, dobutamine or other inotrope-related stress-test echocardiography) reliably indicate potential for early LV recovery of function following CABG, whereas metabolic investigations (that is, rest-redistribution radionuclide tests or PET) are more intimately related to long-term results. In our study, dobutamine echocardiography and Thallium-201 rest-redistribution scintigraphy showed to be valuable methods to identify HM and predict favourable postoperative outcome. However, predicting the extent and the maintenance of functional improvement remains a difficult task. Indeed, despite objective evidence of adequate quote of HM, perioperative results were not confirmed at late follow-up. Our study did not include a comprehensive evaluation of myocardial histology. As demonstrated by Shivalkar and associates, only structurally preserved and perfused myocytes show substantial postrevascularization recovery [14]. Accordingly, noninvasive evaluation of HM must parallel structural integrity, otherwise neither significant nor durable recovery of LV function, and then patient outcome, can be achieved. Recently, La Canna showed that a simple acquisition of a basic echocardiographic parameter, namely preserved diastolic thickness, invariably correlates with successful surgical revascularization [19], having echocardiographic stress test or radionuclide assessment a complementary role in establishing potential of LV recovery. Myocardial wall thickness at echocardiography, indeed, has been shown to correlate well with histological findings obtained at intraoperative biopsy from HM segments [20]. The apparent maintenance of myocardial thickness and myocyte function, either metabolically or pharmacologically evidenced are, therefore, the gold standard for patient selection in this setting.

4.2. Patient survival and mode of death

Surgical revascularization has shown to be superior as compared to medical therapy in patients with impaired LV function either with regards to life expectancy or to LV functional recovery also when HM is not specifically established for patient selection [1–3]. However, long-term information of patients with impaired LV function and HM submitted to CABG are still scarce. Our clinical series represents, therefore, a relevant experience since highly selected patients, with proved myocardial hibernation associated with compromised LV function, were enrolled and prospectively followed up. Patient survival, in our series, was 60% at 8 years, showing a better outcome as compared to previous series, which, however, variably included patients without an established presence of HM at the preoperative assessment. It is, therefore, reassuring that conventional therapy, provided that accurate patient selection is carried out, may still have a primary role in the treatment of ischemic cardiomyopathy. Surgical revascularization appeared to influence also the mode of death, since the majority of late fatal events were due to congestive heart failure whereas a few deaths occurred because of malignant arrhythmia. This finding is in contrast to previously reported data concerning mode of death in patients affected by ischemic cardiomyopathy undergoing surgical revascularization. Indeed, arrhythmia-related events have been related to postoperative deaths in 60–100% of the cases [5,21], or have been commonly associated with late morbidity. In addition, our results should be further highlighted by the lack of any prophylactic therapeutic regimen to reduce or prevent ventricular arrhythmia. We can assume, therefore, that, despite the marked compromise of cardiac function, which is usually considered a predisposing factor to life-threatening arrhythmic events, the presence of revascularized HM in patients with ischemic cardiomyopathy appears to play a protective role by reducing the occurrence of
malignant ventricular arrhythmia and, hence, of sudden deaths.

4.3. Left ventricular recovery of function and heart failure recurrence

Our data confirmed that substantial improvement of contractile performance was shown immediately after revascularizing impaired LV myocardium if adequate amount of HM is present. Nonetheless, the recovery of LV function, in our series, was neither quantitatively uniform nor stable along the time. The explanation for such a variable result may be multifactorial. As previously stated, myocardial structure of the hypocontractile segments plays a critical role in functional recovery, being the limited presence of fibrotic tissue a positive predictor of LV functional improvement following CABG [14]. The presence of well developed coronary collateral net was also shown to

Fig. 5. This figure shows the influence of preoperative angina on postoperative outcome of patients submitted to coronary artery bypass grafting with depressed cardiac function and hibernating myocardium. No difference was found in relation to patient survival (A) or to recurrence of postoperative heart failure (B) when ischemic symptoms were present (yes) or absent (no).
predict restoration of segmental wall motion [22]. Our series showed that CABG procedure in the presence of appropriate extent of HM and positive response to preoperative echocardiographic test accounts for significant LV improvement at short term. Furthermore, patients with worse preoperative LV function had limited perioperative LV recovery, had a rapid decline in improved LVEF, and had more frequent recurrence of heart failure symptoms, high hospital admittance rate, and reduced survival. It can therefore be speculated that patients who had this less than optimal result, despite preoperative assessment of HM, might have had major structural derangement within the akinetic or hypokinetic contractile zones, with expected limited benefit after blood perfusion was restored or with gradual loss of recovered myocardial function due to progressive myocyte degeneration. It appears, therefore, that CABG reduces postoperative death-related events, but does not protect against the progression of ischemic cardiomyopathy in some patients.

The time-limited beneficial effects of CABG in the presence of LV dysfunction was also shown by Luciani, who showed a 47% of patient free from heart failure symptoms at 5 years, despite a 75% of survival at the same follow-up timing [23]. This series, however, included only 48% of patients with preoperative assessment of myocardial viability, making the performance of CABG in patients with irreversibly damaged myocardium likely. It is, therefore, unquestionable that more homogeneous clinical series are still needed to further elucidate the optimal patient selection process in the decision making of ischemic cardiomyopathy, and, on the other hand, it should be taken into account that other determinants may contribute to unfavourable postoperative outcome or to transient benefit of myocardial revascularization. The recurrence of heart failure, for instance, may be due to several factors which have no relation to preoperative patient characteristics: postoperative coronary or myocardial disease progression, incomplete myocardial revascularization with limited reperfusion of potentially recoverable segments, postoperative graft disease, intraoperative-induced myocardial damage, are all factors which may act singly or in combination limiting or hampering the benefits obtained by the CABG procedure. It is conceivable that the etiology of patient death and recidivant episodes of heat failure in this peculiar setting may be multifactorial and, as such, extremely complex to disclose.

4.4. The influence of type of CABG conduit

The choice of conduit has been previously shown to influence postoperative morbidity and mortality in routine CABG experiences. The recent trends in CABG procedure have clearly favoured the use of arterial conduits, not only to perfuse the LAD coronary artery, also in patients with impaired cardiac function. Jegaden and coauthors, however, recently reported on potential unfavourable effects of extensive use of arterial grafts as compared to more conventional surgical management (LITA plus vein grafts) to revascularize patients affected by impaired LV function, documenting increased rate of perioperative complications and no benefit as far as survival was concerned [24]. The lack of benefit by using arterial grafts to perfuse ischemic cardiomyopathy was shown by other investigators [1,25]. Conversely, Luciani and coworkers showed that the use of LITA grafts appeared to be a positive predictor of reduced heart failure events or recurrence in patients with depressed LV performance [23]. This is in contrast to our findings since we could not document any benefit in terms of life expectancy, heart failure or angina recurrence in patients with LV dysfunction and HM when arterial grafts were used. Attrition rate of CABG conduits may affect recovery of myocardial function, but no reports, to our knowledge, have shown reduced benefit of CABG procedure in this particular setting or have objectively documented heart failure recurrence due to recidivant myocardial dysfunction or hibernation secondary to graft disease. On the other hand, longest follow-up in our study was limited to 9 years, and benefits from arterial revascularization are well known to exert an impact on a longer run. Recatheterization is, however, underway at our Institution and will hopefully provide meaningful insights on potential correlation between graft disease, and thus, benefit of arterial grafts, and postoperative outcome at medium and long term.

4.5. Preoperative predictors of late outcome

The complexity of accurately identifying additional predictors, other than the presence and extent of HM, is self-explanatory in patients who usually present several additional risk factors for unfavourable post-CABG results. Preoperative symptoms have been claimed to be associated with postoperative outcome. The presence of angina has been shown to predict better survival rate and more consistent improvement in LV function [7]. However, Di Carli and collaborators showed that also patients with depressed LV function and no or minimal anginal symptoms undergoing surgical revascularization did better than patients treated medically, despite results were less favourable than the angina group, provided that PET mismatch could be detected in akinetic areas1. In this study, however, viability assessment was not performed in all patients, with obvious implication on patient selection. Our study population, which included exclusively patients with evidence of HM, showed no difference in terms of mortality or heart failure recurrence regardless the presence of ischemic-related symptoms. These findings are in accordance with the study reported by Dreyfus who showed the importance of viability tests instead of clinical evaluation as crucial determinant for effective patient selection and subsequent postoperative outcome [26]. However, our study did show that preoperative heart failure symptoms and advanced impairment of functional capacity were independent predictors of poor prognosis, although HM was invariably detected in all the selected patients. This apparently contradictory finding stresses, once again, the importance of adding additional
cles with regards to the need of obtaining more accurate information about extent of myocyte structural derangement. It is arguable that advanced heart failure conditions be more likely associated with wider areas of irreversible structural abnormalities and smaller amount of preserved yet hibernated myocyte structure.

Our study showed also that increased age was a significant predictor of unfavourable outcome, like previously demonstrated by other investigators [27,28], making the therapeutic decision making in elderly patients affected by ischemic cardiomyopathy extremely controversial since other additional alternatives, like heart transplantation, would also be contraindicated.

4.6. Study limitations

This series represents a prospective non-randomized study. Patients were selected exclusively for CABG procedure and according to the presence of adequate amount of HM. Therefore, they were not randomly assigned to different type of therapeutic management. Changes in operative strategies along the study course also occurred and, thus, may have influenced postoperative results and related data interpretation. Postoperative assessment was not complete in regards to quality of coronary revascularization and graft patency, since not all patients were submitted to recatheterization along the follow-up, making the interpretation of causes of unfavourable outcome potentially misleading if merely directed to preoperative factors since relevant postoperative factors might have intervened with marked impact on patient survival and LV function. Echocardiographic assessments were all performed by two experienced echocardiographers (G. L.C., C. C.), but no intra-observer variation was performed with potential influence on echocardiographic data interpretation.

In conclusion, our findings indicate that, despite LV dysfunction, the presence of HM confers low postoperative mortality and LV functional benefits to patients submitted to CABG. The advantage of CABG to perfuse functionally impaired myocardium in selected patients may also encompass an anthyrrhythmic effect, since a few sudden deaths were encountered, as compared to patients with chronic heart failure medically treated or surgically treated where HM was not detected. Several preoperative factors, however, may account for transient LV recovery of function with subsequent reappearance of heart failure. Furthermore, the perioperative augmentation of LVEF, even if remarkable, appears to be hardly maintained over the time with a trend towards progressive reduction of the LV hemodynamic performance, and the underlying mechanism warrant further investigation. Conduit choice for coronary bypass did not represent, in our study, a critical factor in patient outcome if LV impairment is present. Recent developments in diagnostic assessments will ensure adjunctive information for more appropriate patient selection in this complex settings and, therefore, better postoperative results and account for more favourable allocation of alternative therapeutic resources.

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References

Appendix A. Conference discussion

**Dr. P. Sergeant** (Leuven, Belgium): I have two questions and I would like to ask them in a consecutive fashion and allow you to answer each one first.

We were a little bit disappointed, probably you also, at the loss of gain after a few months after surgery. What is your analysis of that observation?

**Dr. Lorusso**: Absolutely. Thank you for your question and comment. I do think that these patients are a little bit peculiar in this respect. Whenever you have a failure, whatever, I mean, a recurrence of arterial symptom, recurrence of angina, they are not submitted to an aggressive diagnostic process, because they say, well, what we could gain is death, so if nothing happens we cannot do that much. But probably it is not true. We should investigate again, because probably these patients have only graft disease and then can be again treated.

**Dr. Sergeant**: So we should not wait for a return of left ventricular failure, we should not wait for events, but just reanalyze and make new observations?

**Dr. Lorusso**: Sure.

**Dr. W. Flameng** (Leuven, Belgium): There is not much known about the late outcome of hibernating myocardium after revascularization. You might be aware that we published a few years ago an extensive study in circulation where we correlated the ultrastructure of the hibernating myocardium with functional outcome after grafting. We found that in the hibernating myocardium there are two subpopulations. One subpopulation is characterized by a completely normal myocardium and the other by an increase in extracellular matrix surrounding the viable myocytes. I guess that it is mainly in this population of patients you see the bad outcome after revascularization. We could define them preoperatively by PET scanning: these patients do not have the classical mismatch.

Do you have any data on that?

**Dr. Lorusso**: Of course your paper is a key reference in my manuscript. We did as well histologic assessment of these patients, and we found, of course, that the patient who had less benefit had a higher degree of apoptosis in the portion of hibernating myocardium areas. Unfortunately we do not have PETs, and so the assessment, the tools we had to screen these patients were again echocardiography and radio nucleoid studies but I totally agree with you that with the PET mismatch and with the structural analysis of these patients we could probably further improve the identification of the patient or, let’s say, the reason why some patients had such a temporary improvement and not maintain a stable increase in left ventricular ejection fraction.

**Dr. A. El Banna** (Cairo, Egypt): Thank you for the nice presentation. The first question is, do you suggest using an intra-aortic balloon during induction of anesthesia with poor ventricular function or not?

The second question is, if you have scars in the myocardium, do you suggest using volume reduction techniques to help these patients?

**Dr. Lorusso**: Thank you for your questions. First of all, this data about perioperative outcome will be presented in the afternoon, but nevertheless, I can tell you that I think we should use a little bit more the intra-aortic balloon pump, especially in the patients, of course, with a more delicate, unstable hemodynamic situation and with a poor left ventricular ejection fraction, just because you would like to reduce as much as possible the negative event in the perioperative phase, like acute myocardial infarction, which, unfortunately we cannot give an answer in this respect, could play a role, an additional role, in the outcome of these patients, because of course you can have some damage. So what you can gain by CABG you can lose by inducing a perioperative myocardial infarction. So I think in the peculiar patient setting I would use more the intra-aortic balloon pump, preoperatively and postoperatively.

As far as the second question, sorry?

**Dr. El Banna**: Do you adopt volume reduction techniques?

**Dr. Lorusso**: No. We used just one case, but so far we did not have experience in this respect. I believe that it can be an adjunct in your armamentarium, but still we do not have any evidence that this can be important

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References:


in, let’s say, patient outcome. So it is difficult to say. We do not have experience anyhow.

**Dr P. Gerometta (Bergamo, Italy):** I would like to ask you whether the perioperative left ventricular ejection fraction increase could be due to a better medical therapy (i.e. intravenous drug) or intensive care, and if you have any data regarding preoperative mitral insufficiency in these patients: have you systematically treated it or not?

**Dr Lorusso:** Well, as far as mitral insufficiency, we did not have many patients with mitral insufficiency, which could be strange in patients with dilated ventricles. So due to this small number, I cannot give you a definitive conclusion.

And the first one?

**Dr Gerometta:** It was about whether the left ventricular ejection fraction increase could be attributed just to a better medical therapy.

**Dr Lorusso:** I think that you can have many reasons. You know that in the perioperative phase you can have a catecholamine release, which could play even a major role in terms of left ventricular ejection fraction and performance. We tried to analyze the neural hormones produced in a few patients, and I can tell you that there are some trends that show that you have a higher release of catecholamines, which can explain partially why you have such a nice improvement perioperatively, which is not shown at three months, but, still, three months you have a significant increase in the left ventricular performance maintained. So this is not certainly related to an acute release of catecholamines.

So I think that it can be the acute effect of the surgery, the high increase, but this increase is maintained at three months and one year, and then after, you have a decrease. I think the progression of the disease, of the cardiomyopathy, can play a major role in this respect.

**Dr G. Mani (New Delhi, India):** Through the follow-up that we are having in the off-pump group being subjected, I mean patients with poor LV being subjected to off-pump, we are already noticing a difference in their postoperative follow-up, and I was wondering whether this is correlated to the drop in the diastolic pulmonary artery pressure, which we see more obviously in the off-pump surgery as compared to our previous bypass operations. I would like to know your comments.

**Dr Lorusso:** In the discussion of the manuscript we took into consideration the fact that in these patients, of course, probably the off-pump technique could give an additional help; we still don’t know. Because trying to avoid any additional damage due to cardiopulmonary or total myocardial ischemia can be important, too, but certainly we do not have evidence to support that.

And I would say that looking at the patient who develops recurrence of heart failure symptom afterwards due to graft disease, I believe that if you can provide complete revascularization and appropriate revascularization with off-pump, then you can probably do that in these patients, but if you cannot reproduce the same thing you can achieve in the CPB patients, I think it can be really tricky, because then you can have incomplete revascularization or you can have a higher rate of graft diseases, stenosis of the anastomosis. I do not want to say that off-pump is less effective, but you have to take into consideration that you have to be really very complete in revascularizing a hibernating myocardium to have the most benefits, the biggest benefits.